

Abscopal Immunity Achieved via in situ Vaccination Using a Novel Combination of Cryoablation and Interleukin-12

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Motivation

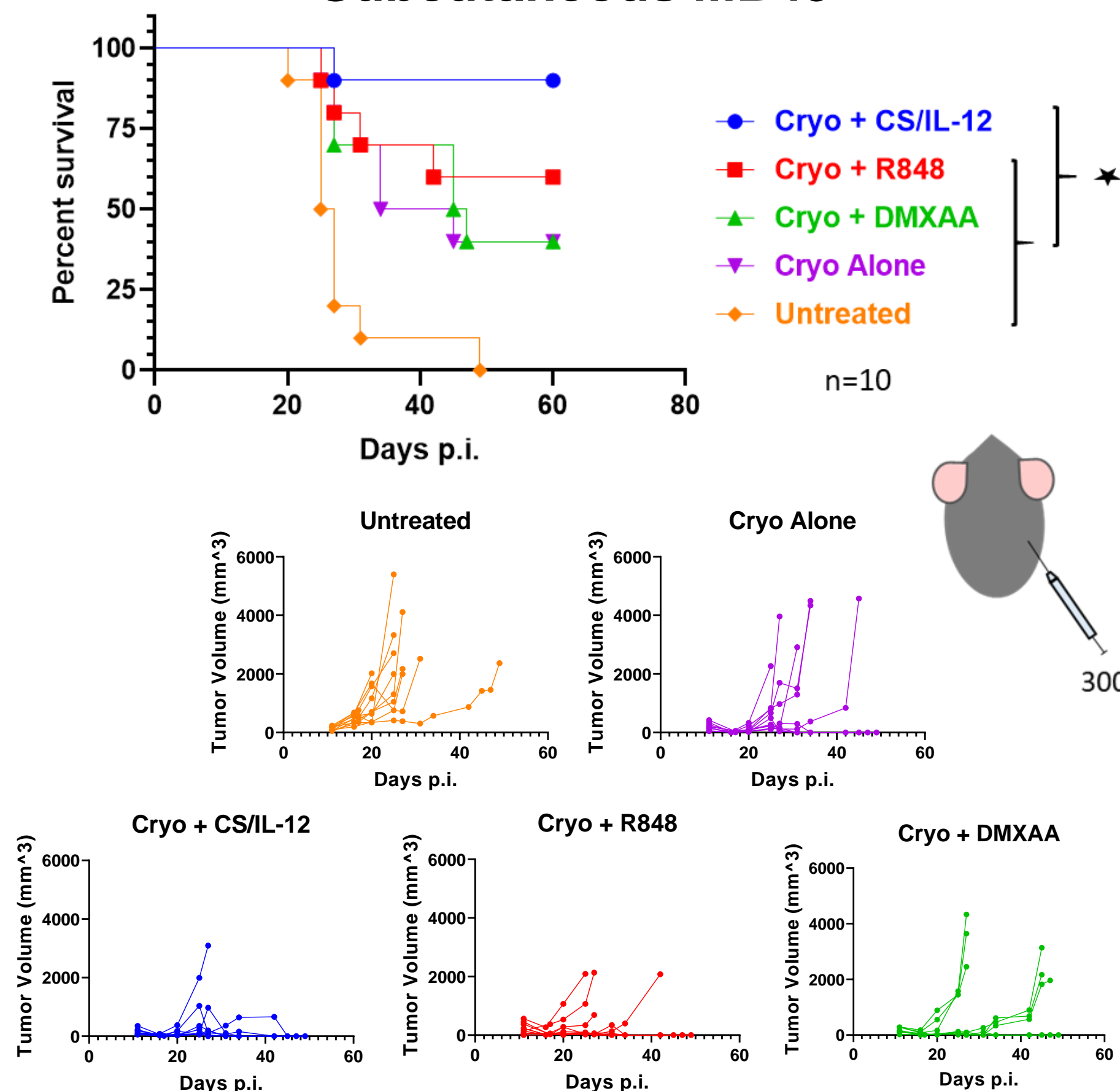
- Clinically, cryoablation is used to treat certain prostate, liver and kidney tumors.
- Because it liberates massive amounts of tumor antigen, cryoablation can potentially serve as an in situ vaccine that is patient- and tumor-specific.
- However, numerous studies report that cryoablation alone rarely provides abscopal immunity [1].
- Hypothesis: Direct injection of an immunomodulator following cryoablation (cryo) can induce tumor-specific immunity, controlling both treated and untreated tumors.

Cryoablation



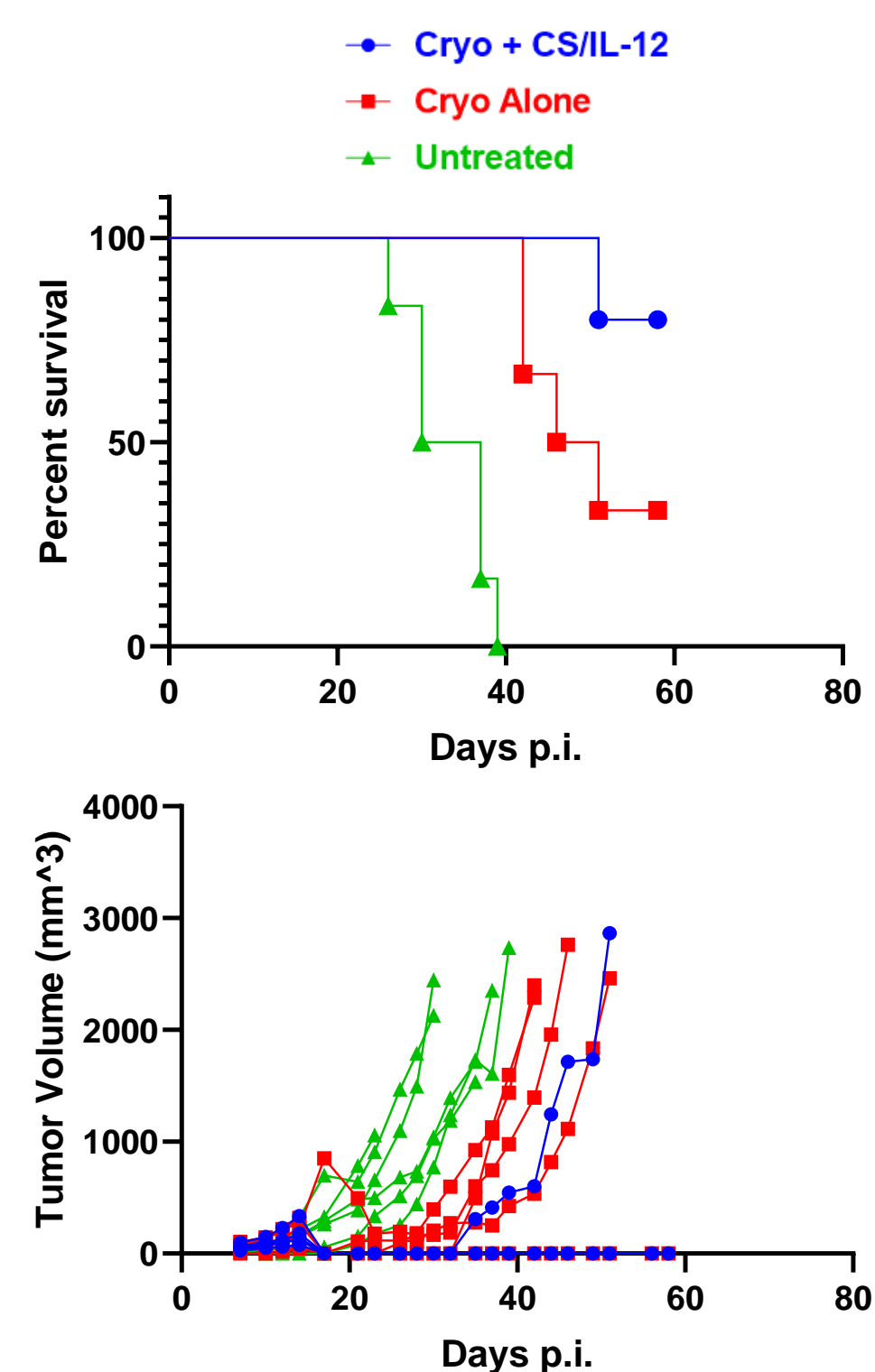
Single Tumor Models

Subcutaneous MB49



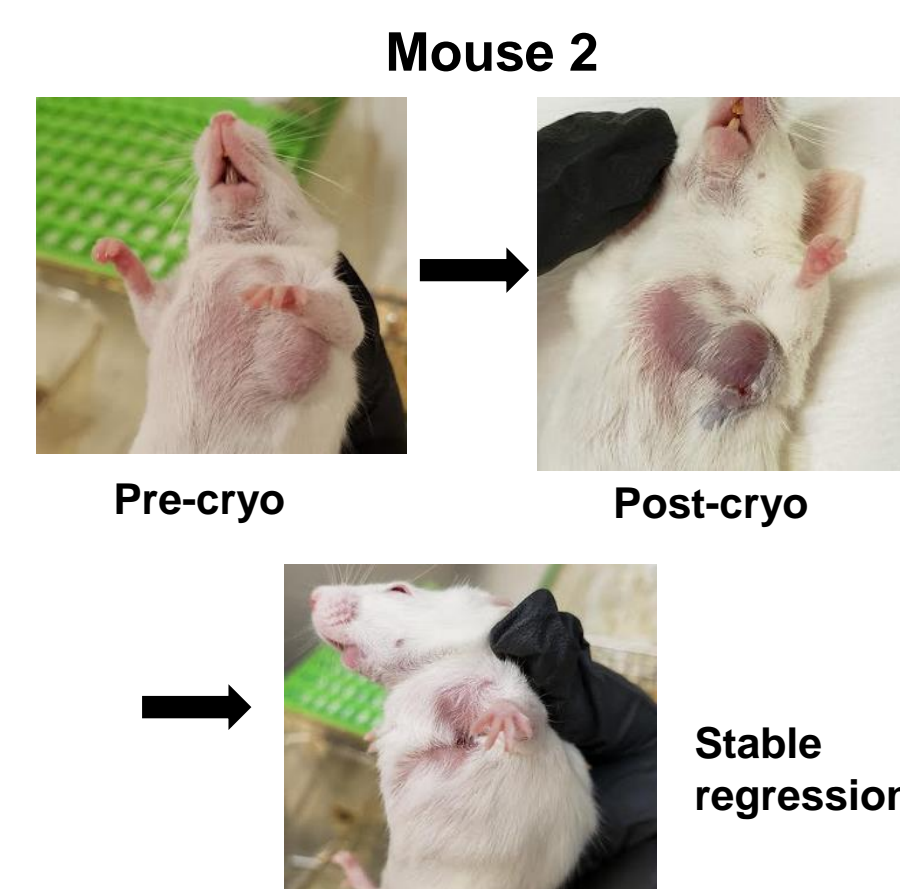
Single Tumor Models

Subcutaneous B16.F10



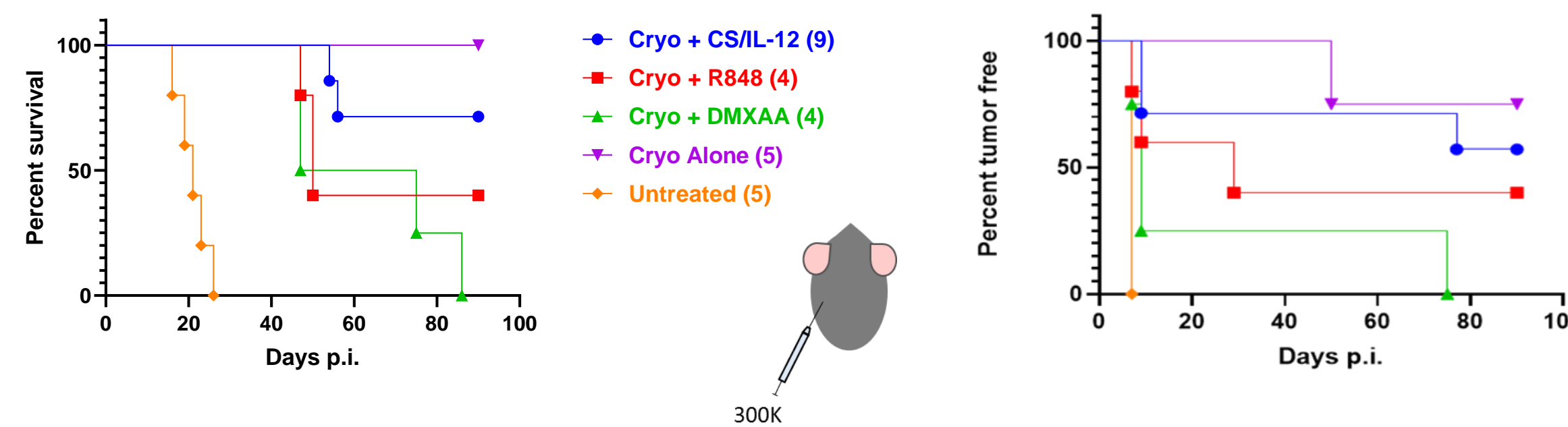
Orthotopic T11

Mouse	M1	M2	M3	M4
Tumor volume at time of cryo	408 mm ³	369 mm ³	732 mm ³	388 mm ³
Dose of CS/IL-12	2 μg, 0 μg, 0 μg	6 μg	6 μg, 6 μg	6 μg
Recryo	2x	-	1x	-
Days of stable regression	euth	55 days	euth	21 days



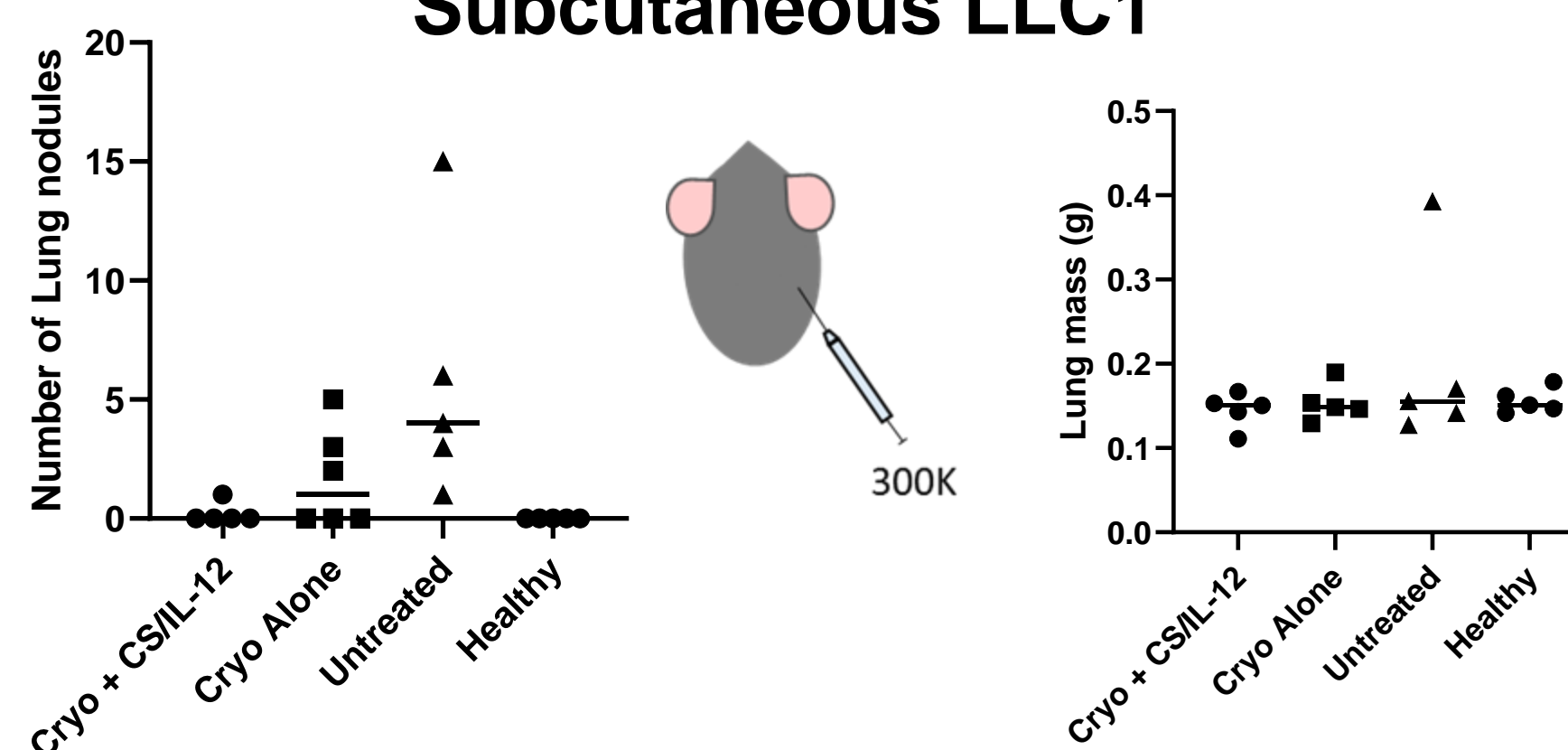
Rechallenge

Subcutaneous MB49



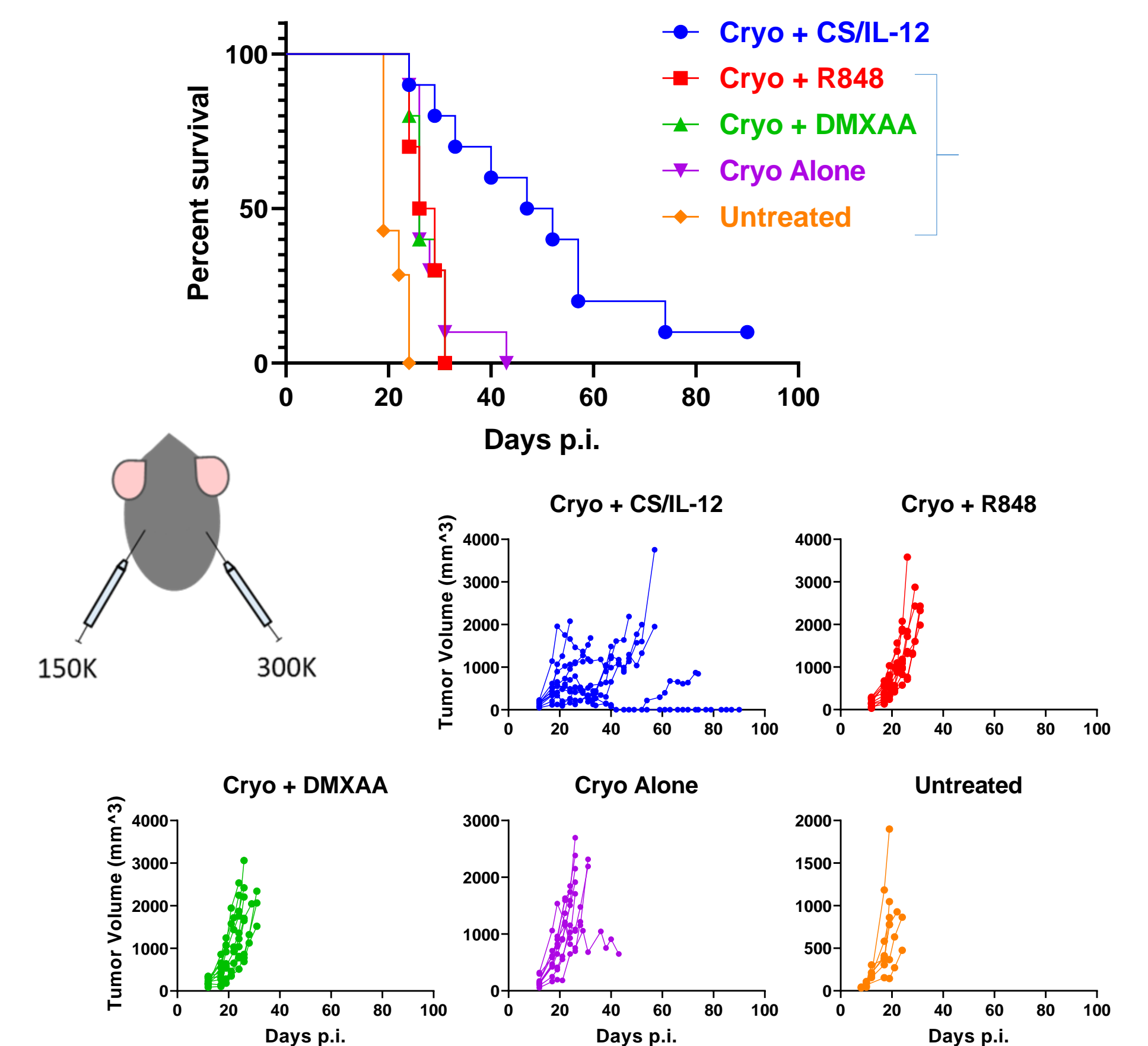
Reduction of Metastases

Subcutaneous LLC1



Abscopal Effect

Subcutaneous MB49



Conclusions

- Cryoablation and local CS/IL-12 (Cryo + CS/IL-12) prevents primary tumor recurrence better than cryo alone or with an agonist, in multiple in vivo tumor models.
- A majority of cured mice in both Cryo + CS/IL-12 and cryo alone groups resisted tumor rechallenge.
- Cryo + CS/IL-12 reduces the number of metastases to the lung compared to untreated controls.
- Cryo + CS/IL-12 significantly slows distant, untreated tumor growth compared to cryo alone or with an agonist.

Future Directions

- What is the composition of the immune cell population before and after cryoablation?
- What role do cytotoxic T lymphocytes play in protective immunity after cryoablation plus immunotherapy?
- What is the mechanism by which loco-regional cryo-immunotherapy inhibits distant tumor growth?
- Does CS/IL-12 improve checkpoint blockade therapy?